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Lower Parel (West)
Mumbai – 400 013

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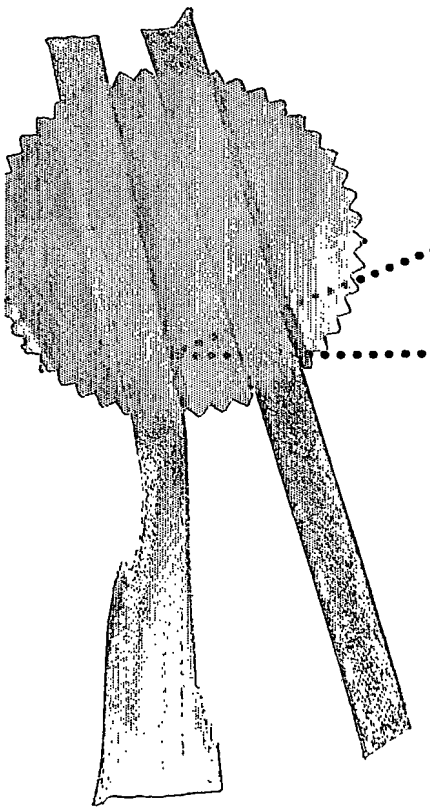
THE PATENTS ACT, 1970

IS HEREBY CERTIFIED THAT, the annex is a true copy of Application and Provisional Specification filed on 23/10/2003 in respect of Patent Application No.1122/MUM/2003 of M/S. CIPLA LIMITED, 289, Bellasis Road, Mumbai Central, Mumbai – 400 008, Maharashtra, India, An Indian Company incorporated under the Companies Act 1956.

This certificate is issued under the powers vested in me under Section 147(1) of the Patents Act, 1970.



Dated this 29th day of Nov 2004.

(R.BHATTACHARYA)
ASST. CONTROLLER OF PATENTS & DESIGNS

FORM 1

THE PATENTS ACT, 1970

(39 of 1970)

APPLICATION FOR GRANT OF A PATENT

[See section 7]

1. We,

   (a) M/S. CIPLA LIMITED

   (b) 289, Bellasis Road, Mumbai Central, Mumbai – 400 008, Maharashtra, India

   (c) Indian company incorporated under the Companies Act 1956

2. Hereby declare –

   (a) that we are in possession of an invention titled **"TRANSDERMAL PHARMACEUTICAL FORMULATIONS"**

   (b) that the Provisional Specification relating to this invention is filed with this application.

   (c) that there is no lawful ground of objection to the grant of a patent to us.

3. Further declare that the inventors for the said invention are

   (a) Lulla, Amar
   (b) 131, Maker Tower-L
   13th Floor, Cuffe Parade
   Colaba, Mumbai 400 015
   Maharashtra, India
   (c) Indian National

   (a) Malhotra, Geena
   (b) 4, Anderson House,
   Opp. Mazgaon Post Office,
   Mazgaon, Mumbai 400 010
   Maharashtra, India
   (c) Indian National

DLPLP
1122/MUM/2003
22-10-03

4. That we are the assignee(s) of the true and first inventors.

5. That our address for service in India is as follows:

GOPAKUMAR NAIR ASSOCIATES, NAIR BAUG, AKURLI ROAD, KANDIVLI (EAST), MUMBAI – 400 101.

6. Following declaration was given by the inventor(s):

We the true and first inventors for this invention in the convention country declare that the applicant(s) herein are our assignee

(Lulla, Amar)

(Malhotra, Geena)

7. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application

8. Following are the attachment with the application:
   (a) Provisional specification (2 copies)
   (b) Statement and Undertaking on Form 3
   (c) Copy of Form 26 (Original Power of attorney in our favour has been submitted with Application No. 168/MUM/2003)
   (d) Fee Rs.3000/- in cheque bearing No.585149 dated 23rd Oct 2003 on Global Trust Bank Limited, Mumbai.

We request that a patent may be granted to us for the said invention.

Dated this the 23rd of, Oct 2003

DR. GOPAKUMAR G. NAIR
Agent for the Applicant
GOPAKUMAR NAIR ASSOCIATES
Nair Baug, Akurli Road,
Kandivli(East) Mumbai – 400

To
The Controller of Patents
The Patent Office,
At Mumbai.

FORM 2

THE PATENTS ACT, 1970

(39 of 1970)

PROVISIONAL SPECIFICATION

[See section 10]

"TRANSDERMAL PHARMACEUTICAL FORMULATIONS"

(a) **CIPLA LTD.**

(b) 289, Bellasis Road, Mumbai Central, Mumbai – 400 008, Maharashtra, India

(c) Indian Company incorporated under the Companies Act 1956

The following specification particularly describes the nature of the invention:

TRANSDERMAL PHARMACEUTICAL FORMULATIONS

FIELD OF THE INVENTION

The invention relates generally to transdermal drug delivery formulations. More specifically, the invention relates to spray formulations for delivering a pharmaceutically active agent to the skin. Any drug suitable for transdermal, transcutaneous or topical administration, including local and systemic active agents, can be used in the present formulations.

BACKGROUND OF THE INVENTION

When technically feasible, topical or transdermal delivery of drugs for both local and systemic indications offers many advantages over oral administration. Benefits of transdermal delivery include increased patient compliance, localized drug targeting, control over rate of absorption and avoidance of reduced bioavailability due to first pass metabolism effects in the liver. Classic topical delivery vehicles include ointments, creams, lotions, pastes and gels.

More recently, controlled-release topical patches have become available. Topical patches are capable of delivering active substances to the skin in a controlled, sustained release manner and have been shown to be effective in the long-term delivery of sustained therapeutic levels of active substances.

There are a few patent prior art in the fields of external preparations for topical administration and transdermal patches. EP0812588 describes such a preparation which aims at inhibiting rejection reactions at organ transplantation or treating autoimmune diseases or allergic diseases.

A transdermal patch for administering a volatile liquid drug such as nicotine transdermally to a patient is described in patent WO0033812.

WO 03035510 discloses a dispenser for conveniently dispensing multiple transdermal transmucosal drug containing patches from a single container.

Emu- oil based formulations in form of a spray or transdermal formula for use as an analgesic, anesthetic and antipruritic is described in US patent no 6528040.

Transdermal patch and topical compositions containing propylnorapomorphine are disclosed in EP patent 1098637 and related patents.

Patent JP 2002 84701 describes a patch for topical treatment of Acne. Topical patch preparation containing a delayed- type hyper sensitivity inducer and methods for using the same are disclosed in patent WO 02072081. Topical anesthetic patch is described in US patent no 6274167.

Patent WO0137890 describes a propellant free spray on skin patch composition for improving wound healing and for drug administration. EP 560014, EP6400352 and EP409550 are among the main prior art documents cited in the search report of the patent WO 0137890.

The above prior art indicate the recent increased attention in transdermal patches however, topical patches can be relatively expensive to produce, and often exhibit reduced adhesion to the skin over time. Irritation has been known to result from patch removal or from adhesive residues left on the skin. Moreover, after use, patches require that appropriate measures be taken to assure safe disposal in order to prevent danger to children or animals.

A number of topical formulations for transdermal delivery of pharmaceuticals have been proposed. However, each of these prior formulations are substantially aqueous solutions

and are limited in that they are only suitable for the delivery of water-soluble drugs. Moreover, although they form non-flowing gels that adhere to skin at body temperature, said gels remain wet to the touch on the skin and can be easily wiped away unless covered with a dressing, thereby requiring the subject to avoid contact with the treated area.

SUMMARY OF THE INVENTION

In a first aspect, the invention provides a transdermal spray formulation comprising a pharmaceutically active agent, a synthetic block copolymer of ethylene oxide and propylene oxide and a non-aqueous vehicle, wherein the non-aqueous vehicle comprises at least about 60% of the formulation.

Also provided does a method of administering a pharmaceutically active agent comprise spraying the transdermal formulations of the invention onto the skin of a subject in need thereof.

In yet another aspect, the invention provides a method of forming a pharmaceutically active film comprising spraying a transdermal formulation comprising an effective amount of a pharmaceutically active agent, a synthetic block copolymer of ethylene oxide and propylene oxide and a non-aqueous vehicle on the skin of a subject in need thereof.

DETAILED DESCRIPTION

The present invention provides transdermal drug delivery formulations. More specifically, the invention relates to spray formulations for delivering a pharmaceutically active agent to the skin. In addition to the pharmaceutically active agent, formulations of the invention comprise a synthetic block copolymer of ethylene oxide and propylene oxide and a non-aqueous vehicle that volatilizes at mammalian body temperature. Upon application, the present formulations quickly dry to produce a film patch containing the active agent in finely dispersed particles. The film patch is easily washable in water. In

some embodiments, patches produced according to the invention provide improved bioavailabilty of the active agent compared to conventionally utilized methods of topical administration.

As used herein, a "pharmaceutically active agent" refers to an agent that produces a biological effect in *in vitro* or *in vivo* systems. The term is intended to include compounds affecting at least one of any therapeutic, prophylactic, pharmacological or physiological response in a subject. More specifically, any active agent that is capable of producing a pharmacological response, either localized or systemic, is within the contemplation of the invention. It should be noted that the active agents may be used singularly or as a mixture of two or more agents or drugs.

As will be understood by those of skill in the art, suitability for transdermal administration of a particular pharmaceutically active agent requires consideration of several factors. For example, prior to incorporating a pharmaceutically active agent in the present formulations, the agent should be evaluated with respect to its permeability through the skin, potential for skin irritation or allergic reaction, pharmacokinetic properties, pharmacodynamic properties, therapeutic window and whether metabolic responses *in vivo* are consistent with continuous administration.

Non-limiting examples of suitable pharmaceutically active agents that may be used in the present transdermal spray formulations may include, but are not limited to, antiinflammatory drugs, analgesics, antiarthritic drugs, antispasmodics, antidepressants, antipsychotics, tranquilizers, antianxiety drugs, narcotic antagonists, antiparkinsonism agents, cholinergic agonists, chemotherapeutic drugs, immunosuppressive agents, antiviral agents, antibiotic agents, appetite suppressants, antiemetics, anticholinergics, antihistaminics, antimigraine agents, coronary, cerebral or peripheral vasodilators, hormonal agents, contraceptives, antithrombotic agents, diuretics, antihypertensive agents, cardiovascular drugs and opioids. Suitable pharmaceutically active agents include both those that are soluble in aqueous media as well as those soluble in non-aqueous media. In accordance with the present invention, the pharmaceutically active

agent is suitably selected from one or more of the group consisting of estradiol, testosterone, oxybutynin, buprenorphine, and fentanyl. Particularly preferred among the suitable compounds is estradiol.

The pharmaceutically active agents of the present invention may be present in an amount up to about 40% by weight of the formulation. Estradiol formulations suitably comprise about 1% to about 5% of estradiol by weight of the formulation.

The pharmaceutically active agents contained in the present formulation may suitably be included in a variety of forms, depending on the solubility and release characteristics desired. Non-limiting examples of suitable forms include neutral molecules, components of molecular complexes, and pharmaceutically acceptable salts, free acids or bases, or quaternary salts of the same, or as combinations of these. Simple derivatives of drugs such as pharmaceutically acceptable ethers, esters, amides which have desirable retention and release characteristics, and which are easily metabolized at body pH and temperature, may be employed. Enzymes, pro-active forms or pro-drugs are also suitable for use in the present invention.

The formulations of the present invention also comprise one or more block copolymers of ethylene oxide and propylene oxide. Synthetic block copolymers of ethylene oxide and propylene oxide, or "poloxamers," as described in the USP/NF Official Monograph (Pharmacopoeia of the United States 25th Revision, National Formulary, 20th Edition, 2002, pp. 2593-95), incorporated herein by reference in its entirety, have the general formula:

$$HO(C_2H_4O)_a(C_3H_6O)_b(C_2H_4O)_aH$$

Wherein a is about 75 to about 105, and wherein b is from about 25 to about 60. In a preferred embodiment, a is about 101 and b is about 56. In another preferred embodiment, a is about 79 and b is about 28.

Poloxamers for use in the present invention may be chosen based on the weight percent of oxyethylene in the polymer. Preferably, oxyethylene units comprise about 70% to

about 85% by weight of the poloxamer. Suitable poloxamers for use in the present invention are typically provided in solid form prior to incorporation in the present formulations. A preferred poloxamer, commercially available as LUTROL F127 (BASF Corporation), has an average molecular weight of from about 7680 to about 9510. A further suitable poloxamer, commercially available as LUTROL F68 (BASF Corporation), has an average molecular weight of from about 9840 to about 14600. A procedure for the determination of average molecular weight of poloxamers is described in the USP/NF Official Monograph (Pharmacopoeia of the United States 25th Revision, National Formulary, 20th Edition, 2002, pp. 2593-95). In the present formulations, poloxamers may be provided in such quantity that the formulation is a liquid below mammalian skin temperature, i.e. about 33°C to about 35°C. Poloxamers exhibit inverted thermoreversibilty, i.e., they dissolve to form a freely flowing liquid at low temperatures and form a semi-solid gel when warmed to body temperature.

Suitably, poloxamers are present in an amount from about 0.1% to about 20% of the formulation by weight. Preferably, poloxamers are present in an amount from about 0.1% to about 5% of the formulation by weight. More preferably, poloxamers are present in an amount from about 0.1% to about 2% of the formulation by weight.

The formulations of the present invention may also comprise of PVP VA copolymers instead of poloxamers. PVP/VA series products play a good role in film-former. Its hygroscopicity decreases with the increase of the proportion of vinylacetate in the molecular. This property of PVP/VA is extremely useful as it works in sprays and lotions. Also, PVP/VA copolymers are primary film formers for a variety of products which demand different degrees of water resistance including aerosol, aqueous, and organic solvent systems. These polymers exhibit film flexibility, good adhesion, luster, water remoistenability, and hardness.

The formulations of the present invention also comprise a non-aqueous vehicle. As used herein, "non-aqueous vehicle" is intended to refer to a vehicle that is substantially water-free. "Substantially water-free," as the term is used herein, means that water comprises

less than about 10% by weight of the total vehicle. Suitably, water comprises less than about 5% of the total vehicle by weight. Most suitably, water comprises less than about 1% of the total vehicle by weight. Vehicles suitably used in accordance with the present invention are non-aqueous solvents that are volatile at mammalian skin temperature, i.e, about 33°C to about 35°C. Upon application to the skin, the solvent evaporates, leaving a film of poloxamer in which the active agent is dispersed as fine particles available for transdermal absorption. Non-limiting examples of suitable non-aqueous solvents include ethanol, acetone and methylal, and mixtures thereof.

In accordance with the invention, the type and amount of non-aqueous vehicle used for a given formulation will depend upon several factors, including the solubility of the pharmaceutically active agent. Particularly suitable non-aqueous vehicles solublilize both the pharmaceutically active agent and the poloxamer.

The non-aqueous vehicle used in the present formulations should be present in an amount from at least about 60% by weight of the formulation. In some embodiments, the non-aqueous vehicle comprises at least about 70%, at least about 80% or at least about 90% by weight of the formulation.

The formulations of the present invention may also comprise additional components, such as anti-nucleating agents and penetration enhancers. As used herein, the term "anti-nucleating agent" refers to any material included in the formulation to prevent crystallization of the pharmaceutically active agent from the non-aqueous vehicle. Suitably, the anti-nucleating agent should be present in an amount from about 1% to about 10% of the formulation by weight. In a preferred embodiment, the anti-nucleating agent comprises about 5% of the formulation by weight. A suitable anti-nucleating agent useful in the present invention is polyvinylpyrrolidone. The term "polyvinylpyrrolidone" or "PVP" refers to a polymer, either a homopolymer or copolymer, containing vinylpyrrolidone (also referred to as N-vinylpyrrolidone, N-vinyl-2-pyrrolidone and N-vinyl-2-pyrrolidinone) as a monomeric unit. PVP polymers include soluble and insoluble homopolymeric PVPs, and copolymers such as vinylpyrrolidone/vinyl acetate and

vinylpyrrolidone/dimethylamino-ethylmethacrylate. The cross-linked homopolymer is insoluble and is generally known in the pharmaceutical industry under the designations polyvinylpolypyrrolidone, crospovidone and PVP. The copolymer vinylpyrrolidone-vinyl acetate is generally known in the pharmaceutical industry under the designations Copolyvidon(e), Copolyvidonum or VP-VAc. A suitable PVP for use in the present invention is known in the art as PVP K-30. Suitably, PVP K-30 is included in an amount from about 1% to 10% of the formulation by weight.

The present formulations may also comprise agents known to accelerate the delivery of the pharmaceutically active agents through the skin. These agents have been referred to as penetration or permeation enhancers, accelerants, adjuvants and absorption promoters, and are collectively referred to herein as "penetration enhancers." Penetration enhancers are suitably provided in an amount from about 0.01% to about 5.0% of the formulation.

Examples of penetration enhancers suitable for use in the present invention are monohydric alcohols such as ethanol and isopropyl, butyl and benzyl alcohols, or dihydric alcohols such as ethylene glycol, diethylene glycol, or propylene glycol, dipropylene glycol and trimethylene glycol, or polyhydric alcohols such as glycerin, sorbitol and polyethylene glycol, polyethylene glycol ethers of aliphatic alcohols (such as cetyl, lauryl, oleyl and stearyl) including polyoxyethylene (4) lauryl ether, polyoxyethylene (2) oleyl ether and polyoxyethylene (10) oleyl ether; vegetable, animal and fish fats and oils such as olive and castor oils, squalene, and lanolin; fatty acid esters such as propyl oleate, decyl oleate, isopropyl palmitate, glycol palmitate, glycol laurate, dodecyl myristate, isopropyl myristate and glycol stearate; fatty acid alcohols such as oleyl alcohol and its derivatives; fatty acid amides such as oleamide and its derivatives; urea and urea derivatives such as allantoin; polar solvents such as dimethyllaurylamide, dodecylpyrrolidone, isosorbitol, salicylic acid; amino acids and higher molecular weight aliphatic surfactants such as lauryl sulfate salts and esters of sorbitol and sorbitol anhydride such as polysorbate 20, which is commercially available under the trademark TWEEN 20, as well as other polysorbates such as 21, 40, 60, 61, 65, 80, 81, and 85. Other enhancers include oleic and linoleic acids, ascorbic acid, panthenol, butylated

hydroxytoluene, tocopherol, tocopherol acetate, tocopheryl linoleate. Particularly suitable penetration enhancers useful in the present invention include menthol, dimethylisosorbide, glycerylmono-oleate and myristyl lactate.

The formulations of the present invention are generally prepared as follows. The synthetic block copolymer is initially dissolved in the non-aqueous vehicle, followed by addition of the pharmaceutically active agent. If necessary, the solution may be sonicated until the pharmaceutically active agent has dissolved. As will be understood by those of skill in the art, additional or alternative means of dissolving the active agent may be used.

The present invention further encompasses a method of administering transdermal spray formulations. The term "administering," as used herein, is intended to mean any mode of application to a tissue of a subject which results in the physical contact of the formulation with an anatomical site or surface area. The term "subject" is intended to include all warm-blooded mammals, preferably humans.

The term "therapeutically effective amount," as used herein with reference to the pharmaceutically active agent, is intended to mean the amount of active agent sufficient to produce the desired effect, local or systemic, when applied topically over the duration of intended use. In some embodiments, the film is allowed to remain on the skin for about 24 hours. Typically, the pharmaceutically active agent is delivered in a controlled release manner.

With respect to particular active agents, therapeutically effective amounts are known in the literature or may be determined by methods known in the art. Typically, effective amounts range from about 0.1 to about 2,100 mg, depending on the active agents chosen and the site of application. The only upper limit on the amount of the active agent is that the composition should remain substantially free of crystals and that the amount of solvent required for dissolving the active agent should not inhibit the patch-forming properties of the formulation.

As will be understood by those of skill in the art, therapeutic dosage and dosage unit amounts can be estimated by *in vitro* flux data. The concentration as well as the quantity of the active agent per unit area, namely per square or cubic centimeter, can be varied independently in order to achieve the desired therapeutic effect. The thickness of the film patch left on the skin can also be varied. In some embodiments, a metered dose spray apparatus may be used to apply the formulation. A metered dose spray apparatus, when used at a fixed distance, allows for the formation of a uniform thin film on the skin. In certain embodiments, the metered dose spray apparatus can be a non-aerosol spray apparatus.

The invention further provides a method of forming a pharmaceutically active film comprising spraying a transdermal formulation in accordance with the invention on the skin of a subject in need thereof. As used herein, the term "film" refers to a poloxamer film containing a pharmaceutically active agent that forms on the skin after application and subsequent drying. As described herein above, a film is formed upon volatilization of the non-aqueous vehicle shortly after contacting the skin. Preferably, the film coating is formed in about 60 seconds or less.

The following examples are provided to assist in a further understanding of the invention. The particular materials and conditions employed are intended to be further illustrative of the invention and are not limiting upon the reasonable scope thereof.

EXAMPLES

Example 1: Formulation for estradiol transdermal spray (100 mg)

A transdermal spray formulation comprising estradiol as the active agent was prepared by first dissolving the poloxamer (LUTROL F127) in ethanol and subsequently adding and dissolving the active agent. The resulting formulation contained the following components in the following amounts:

Ingredient	Composition
Estradiol	3.3 mg
Poloxamer	0.2 mg
Ethanol	96.5 mg

Example 2: Formulation for estradiol transdermal spray (100 mg)

A transdermal spray formulation comprising estradiol as the active agent was prepared by first dissolving the poloxamer (LUTROL F127) in ethanol and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contained the following components in the following amounts:

Ingredient	Composition
Estradiol	3.3 mg
Poloxamer	0.2 mg
PVP K 30	6.0 mg
Ethanol	90.5 mg

Example 3: Formulation for estradiol transdermal spray (100 mg)

A transdermal spray formulation comprising estradiol as the active agent was prepared by first dissolving the poloxamer (LUTROL F127) in ethanol and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contained the following components in the following amounts:

Ingredient	Composition	Quantity/batch (%w/w)
Estradiol	3.3 mg	3.3%
Poloxamer	0.2 mg	0.2%
PVP K 30	6.0 mg	6.0%

Ethanol	90.5 mg	90.5%

Example 4: Formulation for estradiol transdermal spray (2 mg/spray)

A transdermal spray formulation comprising estradiol as the active agent was prepared by first dissolving the poloxamer (LUTROL F127) in ethanol/acetone and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contained the following components in the following amounts:

Ingredient	**Quantity/batch (%w/w)**
Estradiol base	3.3%
Ethanol	37.58%
Acetone	19.58%
Methylal	37.58%
Glyceryl mono-oleate	0.47%
Myristyl lactate	0.47%
Water	0.47%
Cyclomethicone	0.47%
Poloxamer	0.08%

Example 5: Formulation for estradiol transdermal spray (2 mg/spray)

A transdermal spray formulation comprising estradiol as the active agent was prepared by first dissolving the poloxamer (LUTROL F127) in ethanol/acetone and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contained the following components in the following amounts:

Ingredient	Quantity/batch (%w/w)
PVP K-30	6%
Poloxamer	0.2%
Dimethylisosorbide	5%
Menthol	0.05%
Ethanol	28.5%
Acetone	28.5%
Estradiol	3.25%
Methylal	28.5%

Example 6: Formulation for transdermal spray for oxybutynin

A transdermal spray formulation comprising oxybutynin as the active agent is prepared by first dissolving the poloxamer (LUTROL F127) in ethanol and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contains the following components in the following amounts:

Ingredient	Quantity/batch (%w/w)
Oxybutynin	20.00%
Poloxamer	0.20%
Ethanol	79.80%

Example 7: Formulation for transdermal spray for fentanyl

A transdermal spray formulation comprising fentanyl as the active agent is prepared by first dissolving the poloxamer (LUTROL F127) in ethanol and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contains the following components in the following amounts:

Ingredient	Quantity/batch (%w/w)
Fentanyl	2.5 - 10.00%
Poloxamer	0.20%
Ethanol	97.3 - 89.80%

Example 8: Formulation for transdermal spray for buprenorphine

A transdermal spray formulation comprising buprenorphine as the active agent is prepared by first dissolving the poloxamer (LUTROL F127) in ethanol and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contains the following components in the following amounts:

Ingredient	Quantity/batch (%w/w)
Buprenorphine	20 – 40%
Poloxamer	0.20%
Ethanol	79.8 – 59.8%

Example 9: Formulation for transdermal spray for testosterone

A transdermal spray formulation comprising testosterone as the active agent was prepared by first dissolving the poloxamer (LUTROL F127) in ethanol/acetone and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contained the following components in the following amounts:

Ingredient	Quantity/batch (%w/w)
Testosterone	16.12%
Poloxamer	0.20%
Ethanol	70.97%
Acetone	12.71%

Example 10: Formulation for Transdermal Spray for Testosteron

A transdermal spray formulation comprising testosterone as the active agent was prepared by first dissolving the PVP VA in ethanol/acetone and subsequently adding and dissolving the active agent, followed by the addition of the remaining ingredients. The resulting formulation contained the following components in the following amounts:

Ingredient	**Quantity/batch (%w/w)**
Testosterone	16.66%
PVP VA	0.42%
Ethanol	70.48%
Acetone	12.44%

While the present invention has now been described and exemplified with some specificity, those skilled in the art will appreciate the various modifications, including variations, additions and omissions, that may be made in what has been described. Accordingly, it is intended that these modifications also be encompassed by the present invention.

All patents, publications and references cited herein are hereby fully incorporated by reference. In case of conflict between the present disclosure and incorporated patents, publications and references, the present disclosure should control.

Dated this the 23rd day of Oct, 2003

DR. GOPAKUMAR G. NAIR
Agent for the Applicant

To

The Controller of Patents
The Patent Office,
At Mumbai.